

## Abstract

New mutant forms of human dihydrofolate reductase (DHFR) which have properties superior to the previously disclosed mutants have mutations at both amino acid 22 and amino acid 31. Specific mutant forms are Ser31Tyr22, Ser31Phe22, Gly31Tyr22, Gly31Phe22, Ala31Tyr22 and Ala31Phe22. The mutant DHFR of the invention may be used as a selectable marker, and to modify the genome of human cells, particularly bone marrow cells or peripheral blood stem cells, to render them resistant to chemotherapy using antifolate agents.